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特願2000/126623 2000年4月26日 (26.04.2000) JP
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2文字コード及び他の略語については、定期発行される各PCTガゼットの巻頭に掲載されている「コードと略語のガイドスノート」を参照。

(54) Title: NOVEL PEPTIDES

(54)発明の名称: 新規ペプチド

(57) Abstract: Novel peptides compounds inducing the secretion of growth hormone. Peptide compounds or pharmaceutically acceptable salts thereof having an activity of elevating calcium ion concentration in cells which are characterized in that at least one amino acid has been substituted by a modified amino acid and/or a non-amino acid compound.

(57)要約:

WO 01/07475 A1

成長ホルモンの分泌を誘導する新規ペプチド系化合物を提供する。

細胞内のカルシウムイオン濃度を上昇させる活性を有し、少なくとも一つのアミノ酸が修飾アミノ酸及び/又は非アミノ酸化合物により置換されたことを特徴とするペプチド系化合物又はその薬学的に許容される塩。

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Scope of Claims

1. A peptide compound or pharmaceutically acceptable salt thereof with the following characteristics. At least one amino acid of a peptide having activity that increases the calcium ion concentration within a cell undergoes replacement using a modified amino acid and/or a non-amino acid compound.
2. (a) The peptide compound or pharmaceutically acceptable salt thereof described in Section 1 of the scope of claims containing an amino acid sequence which has (a) the amino acid sequence described in sequence 2 or (b) an amino acid sequence that extends from at least the amino terminal up to number 4 through number 10 in the sequence in question and, where at least one amino acid is missing from the section outside the amino acid sequence in question and to which an amino acid sequence has been substituted or added.
3. The peptide compound or pharmaceutically acceptable salt thereof described in Section 2 of the scope of claims having an amino acid sequence selected from a group composed of the amino acid sequences described in sequence numbers 3, 4, 5, 8, 9, 10, 11, 12, 13, 16, 17, 18, 19, 22 and 23.
4. The peptide compound or pharmaceutically acceptable salt thereof described in Section 2 of the scope of claims having an amino acid sequence selected from a group composed of the amino acid sequences described in sequence numbers 25, 26, 29, 30, 31, 32, 34 and 35.
5. A peptide compound or a pharmaceutically acceptable salt thereof with the following characteristics. The activity of the peptide induces the secretion of growth hormone and increases the calcium ion concentration in a cell. In this peptide, (a) the constituent amino acids have either been modified or not and (b) there is at least one amino acid that has undergone substitution using a non-amino acid compound or not.
6. A peptide compound or pharmaceutically acceptable salt thereof with the following characteristics. The peptide compounds described in Sections 1 and 5 of the scope of claims having amino acid sequences described for sequence numbers 27, 28 and 33.

7. The peptide compound or pharmaceutically acceptable salt thereof described in Section 5 of the scope of claims with [REDACTED] following characteristics. It has (a) the amino acid sequence described in sequence number 2 or (b) at least the amino sequence from the amino terminal up to the number four through number ten amino acid sequences. For those sections outside the amino acid sequences from the amino terminal up to the number four through number ten amino acid sequences, it lacks at least one amino acid and contains an amino acid sequence that was substituted and/or added.
8. The peptide compound or pharmaceutically acceptable salt thereof described in Section 7 of the scope of claims with the following characteristics. It has one amino acid sequence selected from the group made up of the amino acid sequences described in sequence numbers 3, 4, 5, 8, 9, 10, 11, 12, 13, 16, 17, 18, 19, 22 and 23.
9. The peptide compound or pharmaceutically acceptable salt thereof described in Section 7 of the scope of claims with the following characteristics. It has one amino acid sequence selected from the group made up of the amino acid sequences described in sequence numbers 25, 26, 29, 30, 31, 32, 34 and 35.
10. A peptide compound or pharmaceutically acceptable salt thereof described in Sections 1 and 5 of the scope of claims, where the section corresponding to the amino acid sequences from the number one of the amino terminal up to number four are expressed using the following formula.

A – B – C – D –

Where A is an amino acid, a non-amino acid compound or is absent, and where B is an amino acid, a non-amino acid compound or is absent. (Note that molecular chain length "A + B" has a length corresponding to the peptide length.)

C and D may be the same or differ and they represent (a) a modified amino acid, (b) an amino acid with a hydrophobic side-chain or (c) an amino acid with a basic side-chain.

11. The peptide compound or pharmaceutically acceptable salt thereof described in Section 10 of the scope of claims with the following characteristics. "C" is either (a) a modified amino acid into which a saturated or unsaturated alkyl chain or chains having carbon numbers of one or more have been introduced into the alpha carbon of the amino acid through ester, ether, thioether, amide or disulfide bonds by using or not using alkaline groups having a carbon number of one or more, or (b) a modified amino acid into which a saturated or unsaturated alkyl chain with a carbon number of one or more has been introduced into the alpha carbon of the amino acid through ester, ether, thioether, amide or disulfide bonds by using or not using alkaline groups having a carbon number of one or more.

12. In the single amino acid sequence selected from the group made up of the amino acid sequences described in sequence numbers 2, 3, 9, 10, 11, 16, 17, 22, 25, 26, 27, 28, 29, 30 and 31, the section corresponding to the amino acid sequence from the amino terminal up to number one through number four is the peptide compound or pharmaceutically acceptable salt thereof which is the peptide compound described in Sections 10 or 11 of the scope of claims.

13. The peptide compound or pharmaceutically acceptable salt thereof described in Sections 1, 2, 3, 5, 7 or 8 of the scope of claims, in which the modified amino acid is the third amino acid from the amino terminal.

14. The peptide compound or pharmaceutically acceptable salt thereof described in Section 13 of the scope of claims with the following characteristics. The amino acid in the modified amino acid is either serine or cysteine.

15. The peptide compound or pharmaceutically acceptable salt thereof described in Sections 1, 2, 3, 5, 7 or 8 of the scope of claims, which contains a modified amino acid into which either (a) a saturated or unsaturated alkyl chain or chains having carbon numbers of one or more have been introduced into the alpha carbon of the amino acid through ester, ether, thioester, thioether, amide or carbamide bonds by using or not using alkylene groups having a carbon number of one or more, or (b) a modified amino acid into which a saturated or unsaturated alkyl chain with a carbon number of one or more or H has been introduced.

16. The amino acid into which the modified amino acid that is introduced to the alpha carbon of the amino acid is either (a) the saturated or unsaturated alkyl chain or chains having a carbon number of one through ester, ether, thioester, thioether, disulfide, amide, carbamide or thiocarbamide bonds either using or not using alkylene groups with a carbon number of one or more, or (b) the amino acid into which saturated or unsaturated alkyl chains having carbon numbers of one or more are introduced, which are the peptide compounds or pharmaceutically acceptable salts thereof described in Sections 1, 2, 4, 5, 6, 7 9, 10 or 12.
17. The peptide compound or pharmaceutically acceptable salt thereof described in Sections 1, 2, 3, 5, 7 or 8 of the scope of claims that has a modified amino acid that has been modified by ester bonding.
18. The peptide compound or pharmaceutically acceptable salt thereof described in Sections 1, 2, 4, 5, 6, 7, 9, 10, 11 or 12 of the scope of claims, which contains a modified amino acid that was modified when the functional group of the side-chains of the amino acid formed ester bonds.
19. The peptide compound or pharmaceutically acceptable salt thereof described in Section 17 of the scope of claims, which has an amino acid in which the fatty acid has undergone an ester bond to the hydroxyl group of the side-chains of the amino acid.
20. The peptide compound or pharmaceutically acceptable salt thereof described in Section 18 of the scope of claims, which has an amino acid in which the fatty acid has undergone thioester bonding to the mercapto group or ester bonding to the hydroxyl group of the side-chains of the amino acid.
21. The peptide compound or pharmaceutically acceptable salt thereof described in Section 19 of the scope of claims, which has an amino acid in which bonded fatty acid has a carbon number from 2 to 35.
22. The peptide compound or pharmaceutically acceptable salt thereof described in Section 20 of the scope of claims, in which the fatty acid has a carbon number from 2 to 35.
23. The peptide compound or pharmaceutically acceptable salt thereof described in Section 21 of the scope of claims, which has

an amino acid in which the bonded fatty acid is selected from a group of fatty acids having carbon numbers of 2, 4, 6, 8, 10, 12, 14, 16 and 18.

24. The peptide compound or a pharmaceutically acceptable salt thereof described in Section 22 of the scope of claims, which is a fatty acid selected from a group composed of the fatty acids having carbon numbers of 2, 4, 6, 8, 10, 12, 14, 16 and 18.

25. The peptide compound or a pharmaceutically acceptable salt thereof described in Section 23 of the scope of claims in which the bonded fatty acid is an octanoic acid, its monoeno fatty acid, or its polyen fatty acid.

26. The peptide compound or a pharmaceutically acceptable salt thereof described in Section 24 of the scope of claims in which the fatty acid is an octanoic acid, its monoeno fatty acid, or its polyen fatty acid.

27. The peptide compound or a pharmaceutically acceptable salt thereof described in Section 23 of the scope of claims in which the bonded fatty acid is a decanoic acid, its monoeno fatty acid, or its polyen fatty acid.

28. The peptide compound or a pharmaceutically acceptable salt thereof described in Section 24 of the scope of claims in which the fatty acid is a decanoic acid, its monoeno fatty acid, or its polyen fatty acid.

29. A peptide compound with the following characteristics. Additional basic amino acids bond to the carboxyl terminal of the peptide compounds described in Sections 1 through 28 of the scope of claims.

30. The peptide compounds described in Sections 1, 2, 3, 5, 7, 8, 13, 14, 15, 17, 19, 21, 23, 25 and 27 of the scope of claims with the following characteristics. The amino terminal is modified using a saturated or unsaturated alkyl or acyl group with a carbon number of one or more and/or, the OH of the carboxyl group at the carboxyl terminal is OZ or NR2R3 (where Z is a pharmaceutically acceptable positive ion or a low-

grade branching chain or a non-branching chain alkyl group, and R2 and R3 are selected from a group made up of H and low-grade branching chains or non-branching chain alkyl groups, which may indicate groups identical to or different from each other).

31. The peptide compounds described in Sections 1, 2, 4, 5, 6, 7, 9, 10, 11, 12, 16, 18, 20, 22, 24, 26, 28 or 29 of the scope of claims with the following characteristics. The amino terminal amino group is modified by introducing a saturated or unsaturated alkyl or acyl group with a carbon number of one or more and/or, the OH of the carboxyl group at the carboxyl terminal is OZ or NR2R3 (where Z is a pharmaceutically acceptable positive ion or a low-grade branching chain or a non-branching chain alkyl group, and R2 and R3 are selected from a groups made up of H and low-grade branching chains or non-branching chain alkyl groups, which may indicate groups identical to or different from each other).
32. A peptide compound with the following characteristics. An additional basic group has been introduced to the amide inducer of the carboxyl terminal of the peptide compounds described in Sections 30 and 31 of the scope of claims.
33. A pharmaceutical compound having as its active ingredient the peptide compounds or pharmaceutically acceptable salts thereof described in Sections 1 through 32 of the scope of claims.
34. A pharmaceutical compound for the purpose of treating illnesses caused by a deficiency of or a decrease in growth hormone having, as its effective ingredient the peptide compounds or pharmaceutically acceptable salts thereof described in Sections 1 through 32 of the scope of claims.
35. A pharmaceutical compound for the purpose of treating illnesses not caused by a deficiency of or a decrease in growth hormones, containing the peptide compounds or pharmaceutically acceptable salts thereof described in Sections 1 through 32 of the scope of claims and a treatment agent pertaining to illnesses not caused by a deficiency of or a decrease in growth hormone.
36. The pharmaceutical compound described in Sections 33 through 35 of the scope of claims for the purpose of applications on non-human animals.
37. A method of treating illnesses caused by a deficiency of or a decrease in growth hormones involving

the administration of pharmaceutical compounds, the active ingredient of which is a peptide compound described in Sections 1 through 32 of the scope of claims or the pharmaceutically acceptable salts thereof.

38. An agent for treating illnesses not caused by a deficiency of or a decrease in growth hormone and a method of treating illnesses not caused by a deficiency of or a decrease in growth hormone involving the administration of pharmaceutical compounds containing a peptide compound or the pharmaceutically acceptable salts thereof, described in Sections 1 through 32 of the scope of claims.

39. Methods of treatment described in Sections 37 and 38 of the scope of claims for applications on non-human animals.

40. DNA that is encoded with amino acid sequences of the peptide compounds described in Sections 1 through 32 of the scope of claims, where the amino acid sequences coded into said DNA contain DNA that has basic sequences encoding peptides containing recognized sequences for which at least one amino acid is modifiable.

41. The DNA described in Section 40 of the scope of claims where one of the basic sequences is selected from a group made up of the basic sequences described in sequence numbers 6, 7, 14, 15, 20, 21, 24, 36, 37, 38, and 39.

42. The DNA described in Section 40 of the scope of claims where one of the basic sequences is selected from a group made up of the basic sequences described in sequence numbers 6, 7, 14, 15, 20, 21, 24, 36, 37, 38, and 39 and is a basic sequence encoded with amino acid.

43. A vector having the DNA described in Sections 40 through 42 of the scope of claims.

44. A cell containing the vector described in Section 43 of the scope of claims.

45. A cell capable of producing a peptide with at least one amino acid modified in the amino acid sequence, which is a peptide compound with a vector containing the DNA described in Sections 40 through 42 of the scope of claims as well as the amino acid sequence encoded in said DNA.

46. An antibody for the peptide compounds described in Sections 1 through 32 of the scope of claims.

47. A method of assaying the peptide compounds described in Sections 1 through 32 of the scope of claims with the following characteristics. The antibody described in Section 46 of the scope of claims is used to detect the peptide compounds described in Sections 1 through 32 of the scope of claims.

48. A detection kit for the peptide compounds described in Sections 1 through 32 of the scope of claims with the following characteristics. The antibody described in Section 46 of the scope of claims is used to detect the peptide compounds described in Sections 1 through 32 of the scope of claims.

49. A method of manufacturing the peptide compounds described in Sections 1 through 32 of the scope of claims consisting of collecting the desired peptide compounds from cell cultures that have undergone phenotypic transformations. In this manufacturing method, genetic manipulation is used on the peptide compounds described in Sections 1 through 32 of the scope of claims and host cells capable of modifying the side-chains of at least one amino acid in the peptide are transformed phenotypically using a vector containing the DNA described in Sections 40 through 42 of the scope of claims.

50. A method of manufacturing the peptide compounds described in Sections 1 through 32 of the scope of claims with the following characteristics. After collecting the desired substances from cell cultures that have been phenotypically transformed, select amino acids are modified chemically. In this manufacturing method, genetic manipulation is used on the peptide compounds described in Sections 1 through 32 of the scope of claims and host cells capable of modifying the side-chains of at least one amino acid in the peptide are transformed phenotypically using a vector containing the DNA described in Sections 40 through 42 of the scope of claims.

51. A method of manufacturing the peptide compounds described in Sections 19 through 28 of the scope of claims with the following characteristics. In the method of manufacturing the peptide compounds described in Sections 19 through 28 using genetic manipulation, cells are used which have activity that causes the fatty acids to undergo ester bonding with the hydroxyl groups of the side-chains of the amino acids or to undergo thioester bonding with the mercapto groups.

52. A method of manufacturing the peptide compounds described in Sections 19 through 28 of the scope of claims with the following characteristics. Cells are used having serine-acyl activity that cause fatty acids to

undergo ester bonding with the hydroxyl groups of the side-chains of the serine in the amino acid sequences described in sequence number 8.

53. A method of manufacturing the peptide compounds described in Sections 19 through 28 of the scope of claims with the following characteristics. Cells are used having acyl activity that cause the fatty acid to undergo ester bonding with the hydroxyl groups of the side-chains of the threonine in the amino acid sequence described in sequence number 28.

54. A pharmaceutical compound for the genetic treatment of illnesses caused by a decrease in or lack of growth hormone that works by manifesting peptides having at least one modified amino acid that has activity that increases the calcium ion concentration in the cell. This is accomplished by integrating a vector containing DNA that encodes the amino acid sequence of the peptide compounds described in Sections 1 through 32 of the scope of claims into the cell of the organism.

55. A method of treating illnesses caused by a decrease in or lack of growth hormone with the following characteristics. Peptides having activity that induces the secretion of growth hormones are manifested by integrating vectors containing the DNA that encodes the amino acid sequences of the peptide compounds described in Sections 1 through 32 of the scope of claims into the cells of the organism. The peptides containing the amino acid sequences encoded in said DNA are produced as peptides having recognized sequences in which at least one of the amino acids can be modified.

56. A pharmaceutical compound for the genetic treatment of illnesses that are not caused by a decrease in or lack of growth hormone. This is accomplished by integrating vectors containing DNA in which the amino acid sequences of the peptide compounds described in Sections 1 through 32 of the scope of claims are encoded into the cells of the organism. These have activity which increases the concentration of the calcium ions in the cells and peptides are manifested that have at least one modified amino acid.

57. A method of treating illnesses not caused by a decrease in or lack of growth hormone with the following characteristics. Vectors containing the DNA that encodes the amino acid sequences of the peptide compounds described in Sections 1 through 32 of the scope of claims are integrated into the cells of an organism capable of producing as peptides, peptides having recognized sequences with at least one modifiable amino acid in the amino acid sequence in question. This allows the expression of peptides having activity that induces the secretion of growth hormone.

SEQUENCE LISTING

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<213> Homo sapiens

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35 40 45

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50 55 60

Ala Glu Glu Ala Glu Glu Glu Leu Glu Ile Arg Phe Asn Ala Pro Phe

65 70 75 . 80

Asp Val Gly Ile Lys Leu Ser Gly Ala Gln Tyr Gln Gln His Gly Arg

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35 40 45

Gln Pro Arg Ala Leu Ala Gly Trp Leu Arg Pro Glu Asp Gly Gly Gln

50 55 60

Ala Glu Gly Ala Glu Asp Glu Leu Glu Val Arg Phe Asn Ala Pro Phe

65 70 75 80

Asp Val Gly Ile Lys Leu Ser Gly Val Gln Tyr Gln Gln His Ser Gln

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Ile Cys Ser Leu Leu Leu Ser Met Leu Trp Met Asp Met Ala Met

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aag gaa tcc aag aag cca cca gct aaa ctt cag cca cga gct ctt gaa			192
Lys Glu Ser Lys Lys Pro Pro Ala Lys Leu Gln Pro Arg Ala Leu Glu			
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75	80	85	
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<213> Homo sapiens

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of growth hormone secretagogue

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 Phe Leu Gln Asp Ile Leu Trp Glu Glu Ala Lys Glu Ala Pro Ala Asp
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<213> *Homo sapiens*

<223> Amino acid sequence for human endogenous peptides (27 amino acids) of growth hormone secretagogue

<400> 11

Gly Ser Ser Phe Leu Ser Pro Glu His Gln Arg Val Gln Arg Lys Glu

1 5 10 15

Ser Lys Lys Pro Pro Ala Lys Leu Gln Pro Arg

20 25

<210> 12

<211> 116

50 55 60
Glu Gly Ala Glu Asp Glu Leu Glu Val Arg Phe Asn Ala Pro Phe Asp
65 70 75 80
Val Gly Ile Lys Leu Ser Gly Val Gln Tyr Gln Gln His Ser Gln Ala
85 90 95
Leu Gly Lys Phe Leu Gln Asp Ile Leu Trp Glu Glu Ala Lys Glu Ala
100 105 110
Pro Ala Asp Lys
115

<210> 14

<211> 498

<212> cDNA

<213> *Rattus norvegicus*

<220>

<221> CDS

<222> (31)... (378)

<223> Base sequence of cDNA coding prepro-form of rat endogenous peptides
(27 amino acids) of growth hormone secretagogue

<400> 14

tccagatcat ctgcctcac caccaaggcc atg gtg tct tca gcg act 48
Met Val Ser Ser Ala Thr

1 5

atc tgc agt ttg cta ctc ctc agc atg ctc tgg atg gac atg gcc atg 96
Ile Cys Ser Leu Leu Leu Ser Met Leu Trp Met Asp Met Ala Met

10 15 20

gca ggt tcc agc ttc ttg agc cca gag cac cag aaa gcc cag aga aag 144
Ala Gly Ser Ser Phe Leu Ser Pro Glu His Gln Lys Ala Gln Arg Lys

25 30 35

gaa tcc aag aag cca cca gct aaa ctg cag cca cga gct ctg gaa ggc 192
Glu Ser Lys Lys Pro Pro Ala Lys Leu Gln Pro Arg Ala Leu Glu Gly

40 45 50

ttg ctc cac cca gag gac aga gga caa gca gaa gag gca gag gag gag 240
Trp Leu His Pro Glu Asp Arg Gly Gln Ala Glu Glu Ala Glu Glu Glu

55 60 65 70

ctg gaa atc agg ttc aat gct ccc ttc gat gtt ggc atc aag ctg tca 288

Leu Glu Ile Arg Phe Asn Ala Pro Phe Asp Val Gly Ile Lys Leu Ser
 75 80 85
 gga gct cag tac cag cag cat ggc cgg gcc ctg gga aag ttt ctt cag 336
 Gly Ala Gln Tyr Gln Gln His Gly Arg Ala Leu Gly Lys Phe Leu Gln
 90 95 100
 gat atc ctc tgg gaa gag gtc aaa gag gcg cca gct aac aag 378
 Asp Ile Leu Trp Glu Glu Val Lys Glu Ala Pro Ala Asn Lys
 105 110 115
 taaccaciga caggacttgtt cccctgtatctt tccctcttaag caagaacatca catccagctt 438
 ctgccttcctc tgcacttccc agcactctcc tgcgtacttca caaataaaatg ttcaaggctgt 498

<210> 15
 <211> 508
 <212> DNA
 <220>
 <221> CDS
 <222> (34)... (381)
 <213> Homo sapiens
 <223> Base sequence of cDNA coding prepro-form of human endogenous peptides
 (27 amino acids) of growth hormone secretagogue
 <400> 15

gcaggcccac ctgtctgtcaa cccagctgag gcc atg ccc tcc cca 45
 Met Pro Ser Pro
 1
 ggg acc gtc tgc agc ctc ctg ctc ggc atg ctc tgg ctg gac ttg 93
 Gly Thr Val Cys Ser Leu Leu Leu Gly Met Leu Trp Leu Asp Leu
 5 10 15 20
 gcc atg gca ggc tcc agc ttc ctg agc cct gaa cac cag aga gtc cag 141
 Ala Met Ala Gly Ser Ser Phe Leu Ser Pro Glu His Gln Arg Val Gln
 25 30 35
 aga aag gag tgc aag aag cca cca gcc aag ctg cag ccc cga gct cta 189
 Arg Lys Glu Ser Lys Lys Pro Pro Ala Lys Leu Gln Pro Arg Ala Leu
 40 45 50
 gca ggc tgg ctc cgc ccg gaa gat gga ggt caa gca gaa ggg gca gag 237
 Ala Gly Trp Leu Arg Pro Glu Asp Gly Gly Gln Ala Glu Gly Ala Glu
 55 60 65

10/25

gat gaa ctg gaa gtc cgg ttc aac gcc ccc ttt gat gtt gga atc aag 285
 Asp Glu Leu Glu Val Arg Phe Asn Ala Pro Phe Asp Val Gly Ile Lys

70 75 80

ctg tca ggg gtt cag tac cag cag cac agc cag gcc ctg ggg aag ttt 333
 Leu Ser Gly Val Gln Tyr Gln Gln His Ser Gln Ala Leu Gly Lys Phe

85 90 95 100

ctt cag gac atc ctc tgg gaa gag gcc aaa gag gcc cca gcc gac aag 381
 Leu Gln Asp Ile Leu Trp Glu Glu Ala Lys Glu Ala Pro Ala Asp Lys

105 110 115

tgtatcgccca caaggcttac tcacccctct ctaagtttag aagcgctcat 431

ctggcttttc gcttgctct gcagcaactc ccacgactgt tgtacaagct caggaggcga 491
 ataaatgttc aaacigt 508

<210> 16

<211> 28

<212> PRT

<213> Sus scrofa (pig)

<223> Amino acid sequence for porcine endogenous peptides of growth hormone secretagogue

<400> 16

Gly Ser Ser Phe Leu Ser Pro Glu His Gln Lys Val Gln Gln Arg Lys

1 5 10 15

Glu Ser Lys Lys Pro Ala Ala Lys Leu Lys Pro Arg

20 25

<210> 17

<211> 27

<212> PRT

<213> Sus scrofa (pig)

<223> Amino acid sequence for porcine endogenous peptides (27 amino acids) of growth hormone secretagogue

<400> 17

Gly Ser Ser Phe Leu Ser Pro Glu His Gln Lys Val Gln Arg Lys Glu

1 5 10 15

Ser Lys Lys Pro Ala Ala Lys Leu Lys Pro Arg

20

25

<210> 18

<211> 118

<212> PRT

<213> Sus scrofa (pig)

<223> Amino acid sequence for prepro-form of porcine endogenous peptides of growth hormone secretagogue

<400> 18

Met Pro Ser Thr Gly Thr Ile Cys Ser Leu Leu Leu Ser Val Leu
1 5 10 15

Leu Met Ala Asp Leu Ala Met Ala Gly Ser Ser Phe Leu Ser Pro Glu
20 25 30

His Gln Lys Val Gln Gln Arg Lys Glu Ser Lys Lys Pro Ala Ala Lys
35 40 45

Leu Lys Pro Arg Ala Leu Glu Gly Trp Leu Gly Pro Glu Asp Ser Gly
50 55 60

Glu Val Glu Gly Thr Glu Asp Lys Leu Glu Ile Arg Phe Asn Ala Pro
65 70 75 80

Cys Asp Val Gly Ile Lys Leu Ser Gly Ala Gln Ser Asp Gln His Gly
85 90 95

Gln Pro Leu Gly Lys Phe Leu Gln Asp Ile Leu Trp Glu Glu Val Thr
100 105 110

Glu Ala Pro Ala Asp Lys
115

<210> 19

<211> 117

<212> PRT

<213> Sus scrofa (pig)

<223> Amino acid sequence for prepro-form of porcine endogenous peptides (27 amino acids) of growth hormone secretagogue

<400> 19

Met Pro Ser Thr Gly Thr Ile Cys Ser Leu Leu Leu Ser Val Leu
1 5 10 15

Leu Met Ala Asp Leu Ala Met Ala Gly Ser Ser Phe Leu Ser Pro Glu

20	25	30
His Gln Lys Val Gln Arg Lys Glu Ser Lys Lys Pro Ala Ala Lys Leu		
35	40	45
Lys Pro Arg Ala Leu Glu Gly Trp Leu Gly Pro Glu Asp Ser Gly Glu		
50	55	60
Val Glu Gly Thr Glu Asp Lys Leu Glu Ile Arg Phe Asn Ala Pro Cys		
65	70	75
Asp Val Gly Ile Lys Leu Ser Gly Ala Gln Ser Asp Gln His Gly Gln		
85	90	95
Pro Leu Gly Lys Phe Leu Gln Asp Ile Leu Trp Glu Glu Val Thr Glu		
100	105	110
Ala Pro Ala Asp Lys		
115		

<210> 20		
<211> 494		
<212> DNA		
<220>		
<221> CDS		
<222> (9)... (362)		
<213> Sus scrofa (pig)		
<223> Base sequence of cDNA coding prepro-form of porcine endogenous peptides of growth hormone secretagogue		
<400> 20		
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Met Pro Ser Thr Gly Thr Ile Cys Ser Leu Leu Leu Leu		
1	5	10
agc glg ctc ctc aig gca gac ttg gcc atg gcg ggc tcc agc ttc ttg 95		
Ser Val Leu Leu Met Ala Asp Leu Ala Met Ala Gly Ser Ser Phe Leu		
15	20	25
agc ccc gaa cac cag aaa gtg cag cag aga aag gag tcc aag aag cca 143		
Ser Pro Glu His Gln Lys Val Gln Gln Arg Lys Glu Ser Lys Lys Pro		
30	35	40
45		
gca gcc aaa ctg aag ccc cgg gcc ctg gaa ggc tgg ctc ggc cca gaa 191		
Ala Ala Lys Leu Lys Pro Arg Ala Leu Glu Gly Trp Leu Gly Pro Glu		
50	55	60

gac	agt	gtt	gag	gtg	gaa	ggc	acg	gag	gac	aag	ctg	gaa	atc	cggt	ttc	239
Asp	Ser	Gly	Glu	Val	Glu	Gly	Thr	Glu	Asp	Lys	Leu	Glu	Ile	Arg	Phe	
65				70							75					
aac	gcc	ccc	tgt	gtt	ggg	atc	aag	tgt	tca	ggg	gtt	cag	tcc	gac	287	
Asn	Ala	Pro	Cys	Asp	Val	Gly	Ile	Lys	Leu	Ser	Gly	Ala	Gln	Ser	Asp	
80				85						90						
cag	cac	ggc	cag	ccc	ctg	ggg	aaa	ttt	ctc	cag	gac	atc	ctc	tgg	gaa	335
Gln	His	Gly	Gln	Pro	Leu	Gly	Lys	Phe	Leu	Gln	Asp	Ile	Leu	Trp	Glu	
95				100						105						
gag	gtc	act	gag	gcc	ccg	gcc	gac	aag	tgt	tgt	ccc	tgt	gaggcc	ggc	382	
Glu	Val	Thr	Glu	Ala	Pro	Ala	Asp	Lys								
110				115												
cacc	tgt	ttt	ctcc	cagg	cc	ccta	agg	gtt	cacc	tgg	cc	agg	acgt	tcc	actatca	442
caccc	cc	cc	tgc	tgc	tgc	tgc	tgc	tgc	tgc	tgc	tgc	tgc	tgc	tgc	gg	494
<210> 21																
<211> 491																
<212> DNA																
<220>																
<221> CDS																
<222> (9)... (359)																
<213> Sus scrofa (pig)																
<223> Base sequence of cDNA coding prepro-form of porcine endogenous peptides (27 amino acids) of growth hormone secretagogue																
<400> 21																
ctgaggcc atg ccc tcc acg ggg acc att tgc agc ctg ctg ctc ctc															47	
Met Pro Ser Thr Gly Thr Ile Cys Ser Leu Leu Leu Leu																
1		5		10												
agc	gtg	ctc	ctc	atg	gca	gac	tgt	gcc	atg	gct	ggc	tcc	agc	tcc	tgt	95
Ser	Val	Leu	Leu	Met	Ala	Asp	Leu	Ala	Met	Ala	Gly	Ser	Ser	Phe	Leu	
15		20		25												
agc	ccc	gaa	cac	cag	aaa	gtg	cag	aga	aag	gag	tcc	aag	aag	cca	gca	143
Ser	Pro	Glu	His	Gln	Lys	Val	Gln	Arg	Lys	Glu	Ser	Lys	Lys	Pro	Ala	
30		35		40									45			
gcc	aaa	ctg	aag	ccc	ccg	gcc	ctg	gaa	ggc	tgg	ctc	ggc	cca	gaa	gac	191

Ala Lys Leu Lys Pro Arg Ala Leu Glu Gly Trp Leu Gly Pro Glu Asp
 50 55 60
 agt ggt gag gig gaa ggc acg gag gac aag ctg gaa atc cgg ttc aac 239
 Ser Gly Glu Val Glu Gly Thr Glu Asp Lys Leu Glu Ile Arg Phe Asn
 65 70 75
 gcc ccc tgt gat gtt ggg atc aag ttg tca ggg gct cag tcc gac cag 287
 Ala Pro Cys Asp Val Gly Ile Lys Leu Ser Gly Ala Gln Ser Asp Gln
 80 85 90
 cac ggc cag ccc ctg ggg aaa ttt ctc cag gac atc ctc tgg gaa gag 335
 His Gly Gln Pro Leu Gly Lys Phe Leu Gln Asp Ile Leu Trp Glu Glu
 95 100 105
 gtc act gag gcc ccg gcc gac aag tgattgtccc tgagaccgc 379
 Val Thr Glu Ala Pro Ala Asp Lys
 110 115

caccctctgtt ctccccagcct cctaagggtt caccctggctt ccaggacgc tccactatca 439
 caccctggatgc tagcctggga ggtgaataaa cattcagact gg 491

<210> 22

<211> 27

<212> PRT

<213> Bos taurus

<223> Amino acid sequence for bovine endogenous peptides (27 amino acids) of growth hormone secretagogue

<400> 22

Gly Ser Ser Phe Leu Ser Pro Glu His Gln Glu Leu Gln Arg Lys Glu

1 5 10 15

Ala Lys Lys Pro Ser Gly Arg Leu Lys Pro Arg

20 25

<210> 23

<211> 89

<212> PRT

<213> Bos taurus

<223> Partial amino acid sequence for a prepro-form of bovine endogenous peptides (27 amino acids) of growth hormone secretagogue

<400> 23

Asp Leu Ala Met Ala Gly Ser Ser Phe Leu Ser Pro Glu His Gln Glu
 1 5 10 15
 Leu Gln Arg Lys Glu Ala Lys Lys Pro Ser Gly Arg Leu Lys Pro Arg
 20 25 30
 Thr Leu Glu Gly Gln Phe Asp Phe Glu Val Gly Ser Gln Ala Glu Gly
 35 40 45
 Ala Glu Asp Glu Leu Glu Ile Arg Phe Asn Ala Phe Phe Asn Ile Gly
 50 55 60
 Ile Lys Leu Ala Gly Ala Gln Ser Leu Gln His Gly Gln Thr Leu Gly
 65 70 75 80
 Lys Phe Leu Gln Asp Ile Leu Trp Glu
 85

<210> 24

<211> 267

<212> DNA

<220>

<221> CDS

<222> (1)... (267)

<213> Bos taurus

<223> Base sequence of cDNA coding prepro-form of bovine endogenous peptides (27 amino acids) of growth hormone secretagogue

<400> 24

gac ttg gcc atg gcg ggc tcc agc ttt ctg agc ccc gaa cat cag gaa 48
 Asp Leu Ala Met Ala Gly Ser Ser Phe Leu Ser Pro Glu His Gln Glu
 1 5 10 15
 ctg cag aga aag gaa gct aag aag cca tca ggc aga ctg aag ccc cgg 96
 Leu Gln Arg Lys Glu Ala Lys Lys Pro Ser Gly Arg Leu Lys Pro Arg
 20 25 30
 acc ctg gaa ggc cag ttt gac ccg gag gtg gga agt cag gcg gaa ggt 144
 Thr Leu Glu Gly Gln Phe Asp Phe Glu Val Gly Ser Gln Ala Glu Gly
 35 40 45
 gca gag gac gag ctg gaa atc cgg ttc aac gcc ccc ttt aac att ggg 192
 Ala Glu Asp Glu Leu Glu Ile Arg Phe Asn Ala Phe Phe Asn Ile Gly
 50 55 60

atc aag cta gca ggg gct cag tcc ctc cag cat ggc cag acg ttg ggg 240
Ile Lys Leu Ala Gly Ala Gln Ser Leu Gln His Gly Gln Thr Leu Gly
65 70 75 80
aag ttt ctt cag gac atc ctc tgg gaa 267
Lys Phe Leu Gln Asp Ile Leu Trp Glu
85

<210> 25
<211> 24
<212> PRT
<213> Gallus domesticus
<223> Amino acid sequence for chicken endogenous peptides of growth hormone
secretagogue
<400> 25
Gly Ser Ser Phe Leu Ser Pro Thr Tyr Lys Asn Ile Gln Gln Gln Lys
1 5 10 15
Gly Thr Arg Lys Pro Thr Ala Arg
20

<210> 26
<211> 21
<212> PRT
<213> Anguilla japonica
<220>
<221> AMIDATION
<222> 21
<223> Amino acid sequence for eel endogenous peptides of growth hormone
secretagogue
<400> 26
Gly Ser Ser Phe Leu Ser Pro Ser Gln Arg Pro Gln Gly Lys Asp Lys
1 5 10 15
Lys Pro Pro Arg Val
20

<210> 27
<211> 28

<212> PRT

<213> Rana catesbeiana

<223> Amino acid sequence for frog endogenous peptides of growth hormone secretagogue

<400> 27

Gly Leu Ser Phe Leu Ser Pro Ala Glu Met Gln Lys Ile Ala Glu Arg

1 5 10 15

Gln Ser Gln Asn Lys Leu Arg His Gly Asn Met Arg

20 25

<210> 28

<211> 27

<212> PRT

<213> Xenopus laevis

<223> Amino acid sequence for frog (Xenopus laevis) endogenous peptides of growth hormone secretagogue

<400> 28

Gly Leu Thr Phe Leu Ser Pro Ala Asp Met Gln Lys Ile Ala Glu Arg

1 5 10 15

Gln Ser Gln Asn Lys Leu Arg His Gly Asn Met

20 25

<210> 29

<211> 23

<212> PRT

<213> Oncorhynchus mykiss

<220>

<221>AMIDATION

<222> 23

<223> Amino acid sequence for rainbow trout endogenous peptides (23 amino acids) of growth hormone secretagogue

<400> 29

Gly Ser Ser Phe Leu Ser Pro Ser Gln Lys Pro Gln Val Arg Gln Gly

1 5 10 15

Lys Gly Lys Pro Pro Arg Val

20

<210> 30

<211> 20

<212> PRT

<213> *Oncorhynchus mykiss*

<220>

<221> AMIDATION

<222> 20

<223> Amino acid sequence for rainbow trout endogenous peptides (20 amino acids) of growth hormone secretagogue

<400> 30

Gly Ser Ser Phe Leu Ser Pro Ser Gln Lys Pro Gln Gly Lys Gly Lys

1

5

10

15

Pro Pro Arg Val

20

<210> 31

<211> 28

<212> PRT

<213> *Canis familiaris*

<223> Amino acid sequence for dog endogenous peptides of growth hormone secretagogue

<400> 31

Gly Ser Ser Phe Leu Ser Pro Glu His Gln Lys Leu Gln Gln Arg Lys

1

5

10

15

Glu Ser Lys Lys Pro Pro Ala Lys Leu Gln Pro Arg

20

25

<210> 32

<211> 108

<212> PRT

<213> *Anguilla japonica*

<223> Amino acid sequence for prepro-form of eel endogenous peptides of growth hormone secretagogue

<400> 32

Met Lys Arg Thr Ala Tyr Ile Ile Leu Leu Val Cys Val Leu Ala Leu

1 5 10 15
Trp Met Asp Ser Val Gln Ala Gly Ser Ser Phe Leu Ser Pro Ser Gln
20 25 30
Arg Pro Gln Gly Lys Asp Lys Lys Pro Pro Arg Val Gly Arg Arg Asp
35 40 45
Ser Asp Gly Ile Leu Asp Leu Phe Met Arg Pro Pro Leu Gln Asp Glu
50 55 60
Asp Ile Arg His Ile Thr Phe Asn Thr Pro Phe Glu Ile Gly Ile Thr
65 70 75 80
Met Thr Glu Glu Leu Phe Gln Gln Tyr Gly Glu Val Met Gln Lys Ile
85 90 95
Met Gln Asp Leu Leu Met Asp Thr Pro Ala Lys Glu
100 105

<210> 33

<211> 114

<212> PRT

<213> Xenopus laevis

<223> Amino acid sequence frog (Xenopus laevis) endogenous peptides of growth hormone secretagogue

<400>33

Met Asn Phe Gly Lys Ala Ala Ile Phe Gly Val Val Leu Phe Cys Leu
1 5 10 15
Leu Trp Thr Glu Gly Ala Gln Ala Gly Leu Thr Phe Leu Ser Pro Ala
20 25 30
Asp Met Gln Lys Ile Ala Glu Arg Gln Ser Gln Asn Lys Leu Arg His
35 40 45
Gly Asn Met Asn Arg Arg Gly Val Glu Asp Asp Leu Ala Gly Glu Glu
50 55 60
Ile Gly Val Thr Phe Pro Leu Asp Met Lys Met Thr Gln Glu Gln Phe
65 70 75 80
Gln Lys Gln Arg Ala Ala Val Gln Asp Phe Leu Tyr Ser Ser Leu Leu
85 90 95
Ser Leu Gly Ser Val Gln Asp Thr Glu Asp Lys Asn Glu Asn Pro Gln
100 105 110
Ser Gln

<210> 34

<211> 82

<212> PRT

<213> *Oncorhynchus mykiss*

<223> Amino acid sequence for prepro-form of rainbow trout endogenous peptides (23 amino acids) of growth hormone secretagogue

<400>34

Met Ile Leu Met Leu Cys Thr Leu Ala Leu Trp Ala Lys Ser Val Ser
1 5 10 15
Ala Gly Ser Ser Phe Leu Ser Pro Ser Gln Lys Pro Gln Val Arg Gln
20 25 30
Gly Lys Gly Lys Pro Pro Arg Val Gly Arg Arg Asp Ile Glu Ser Phe
35 40 45
Ala Glu Leu Phe Glu Gly Pro Leu His Gln Glu Asp Lys His Asn Thr
50 55 60
Ile Lys Ala Pro Phe Glu Met Gly Ile Thr Met Ser Glu Glu Glu Phe
65 70 75 80
Gln Glu

<210> 35

<211> 99

<212> PRT

<213> *Oncorhynchus mykiss*

<223> Amino acid sequence for prepro-form of rainbow trout endogenous peptides (20 amino acids) of growth hormone secretagogue

<400>35

Met Ile Leu Met Leu Cys Thr Leu Ala Leu Trp Ala Lys Ser Val Ser
1 5 10 15
Ala Gly Ser Ser Phe Leu Ser Pro Ser Gln Lys Pro Gln Gly Lys Gly
20 25 30
Lys Pro Pro Arg Val Gly Arg Arg Asp Ile Glu Ser Phe Ala Glu Leu
35 40 45
Phe Glu Gly Pro Leu His Gln Glu Asp Lys His Asn Thr Ile Lys Ala
50 55 60
Pro Phe Glu Met Gly Ile Thr Met Ser Glu Glu Glu Phe Gln Glu Tyr

<210> 36
<211> 503
<212> DNA
<220>
<221> CDS
<222> (66)... (389)
<213> *Anguilla japonica*
<223> Base sequence of cDNA coding prepro-form of eel endogenous peptides of growth hormone secretagogue
<400> 36
tcctaaaggc actgggtttc ctcttaaagt gcaaaaccc actgtgagct tcagacataga 60

ggcag atg aaa cgc acc gca tac atc atc ctg ctg gtc tgc gtc ctg	107
Met Lys Arg Thr Ala Tyr Ile Ile Leu Leu Val Cys Val Leu	
1 5 10	
gca ctg tgg atg gac tct gtc cag gct ggc tcc agc ttc ctc agc ccc	155
Ala Leu Trp Met Asp Ser Val Gln Ala Gly Ser Ser Phe Leu Ser Pro	
15 20 25 30	
tca cag aga ccc cag ggg aag gat aag aag cct ccc agg gtt ggc aga	203
Ser Gln Arg Pro Gln Gly Lys Asp Lys Lys Pro Pro Arg Val Gly Arg	
35 40 45	
cga gac tca gat ggg atc ctg gac ctg ttt atg agg ccc cca ttg cag	251
Arg Asp Ser Asp Gly Ile Leu Asp Leu Phe Met Arg Pro Pro Leu Gln	
50 55 60	
gat gaa gac atc aga cac att acg ttt aac act cct ttt gag atc ggg	299
Asp Glu Asp Ile Arg His Ile Thr Phe Asn Thr Pro Phe Glu Ile Gly	
65 70 75	
atc acc atg act gag gag ctg ttc cag caa tat gga gaa gtg atg cag	347
Ile Thr Met Thr Glu Glu Leu Phe Gln Gln Tyr Gly Glu Val Met Gln	
80 85 90	
aag atc atg cag gat ttg ctg atg gac aca cct gcc aaa gag	389

Lys Ile Met Gln Asp Leu Leu Met Asp Thr Pro Ala Lys Glu
 95 100 105
 tgacaagagl ggatatgatc tggacttcat aaaaccctgc gtcccatata tccctgcatt 449
 atlgcatgca taattcaacc aattgttaaa catttaataa aattttgcaa acgc 503

<210> 37
 <211> 484
 <212> DNA
 <220>
 <221> CDS
 <222> (47)... (388)
 <213> Xenopus laevis
 <223> Base sequence of cDNA coding prepro-form of frog
 (Xenopus laevis) endogenous peptides of growth hormone
 secretagogue
 <400> 37
 ttacacttt atctcgagg cggcaccgtt gaccaggacc ttctagg 46

 atg aat ttt ggt aaa gcc gcc atc ttt ggg gtt gtc ttg ttc tgc ctg 94
 Met Asn Phe Gly Lys Ala Ala Ile Phe Gly Val Val Leu Phe Cys Leu
 1 . 5 10 15
 ctg tgg acg gag ggg gcc cag gct ggc ttg acc ttc ctg agt cca gcc 142
 Leu Trp Thr Glu Gly Ala Gln Ala Gly Leu Thr Phe Leu Ser Pro Ala
 20 25 30
 gac atg cag aag att gcg gag agg caa tca cag aat aag ctg aga cac 190
 Asp Met Gln Lys Ile Ala Glu Arg Gln Ser Gln Asn Lys Leu Arg His
 35 40 45
 ggc aat atg aat cgc agg ggt gtg gag gat gac ctg gcc ggg gag gag 238
 Gly Asn Met Asn Arg Arg Gly Val Glu Asp Asp Leu Ala Gly Glu Glu
 50 55 60
 atc ggg gtg acc ttc cct ctg gat atg aag atg acg cag gag cag ttc 286
 Ile Gly Val Thr Phe Pro Leu Asp Met Lys Met Thr Gln Glu Gln Phe
 65 70 75 80
 cag aag cag agg gct gcg gtg cag gac ttc ctg tac tcc tcc ctg ctg 334
 Gln Lys Gln Arg Ala Ala Val Gln Asp Phe Leu Tyr Ser Ser Leu Leu
 85 90 95

tct ctc ggg tca gtg cag gat aca gaa gac aag aat gaa aat cct cag	382		
Ser Leu Gly Ser Val Gln Asp Thr Glu Asp Lys Asn Glu Asn Pro Gln			
100	105	110	
agc caa tgagaatgtat gaaaaatccgc tgcgtciga tgccccccc cgcattgtgt	438		
Ser Gln			
gtctttatata tctctgtata acccagaaaat aaatctttatt tatggc			
484			
<210> 38			
<211> 462			
<212> DNA			
<220>			
<221> CDS			
<222> (12)... (257)			
<213> <i>Oncorhynchus mykiss</i>			
<223> Base sequence of cDNA coding prepro-form of rainbow trout endogenous peptides (23 amino acids) of growth hormone secretagogue			
<400> 38			
tcacaggct c atg ata ctg aig ctg tgt act ctg gct ctg tgg gcc	47		
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aag tca gtc agt gct ggc tcc agc ttc ctc agc ccc tcc cag aaa cca	95		
Lys Ser Val Ser Ala Gly Ser Ser Phe Leu Ser Pro Ser Gln Lys Pro			
15	20	25	
cag gta aga cag ggt aaa ggg aag ccc cct cga gtt ggt cgg cga gac	143		
Gln Val Arg Gln Gly Lys Gly Lys Pro Pro Arg Val Gly Arg Arg Asp			
30	35	40	
att gag agc itt gct gag ctg itt gag ggt ccc ctt cac cag gaa gac	191		
Ile Glu Ser Phe Ala Glu Leu Phe Glu Gly Pro Leu His Gln Glu Asp			
45	50	55	60
aaa cac aat acg atc aag gct cct ttt gag atg ggc atc acc atg agt	239		
Lys His Asn Thr Ile Lys Ala Pro Phe Glu Met Gly Ile Thr Met Ser			
65	70	75	
gag gag gag ttc cag gag tatggtgccg tgcgtcagaa gatccctgcag	287		
Glu Glu Glu Phe Gln Glu			

25/25

acttgtgtgaa catcgtttga attgtaaaaag atgaataaaa taacactgct tcctt 453

INTERNATIONAL SEARCH REPORT

International application No.

PCT/JP00/04907

A. CLASSIFICATION OF SUBJECT MATTER
 Int.Cl' C07K14/47, C12N15/12, C12N1/21, C12P21/02, C07K16/18, A61K38/18,
 A61P5/06, A61P19/08, A61K45/00,
 A61K48/00, G01N33/53

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Int.Cl' C07K14/47, C12N15/12, C12N1/21, C12P21/02, C07K16/18, A61K38/18,
 A61P5/06, A61P19/08, A61K45/00,
 A61K48/00, G01N33/53

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
 SwissProt/PIR/GeneSeq, Genbank/EMBL/DDBJ/GeneSeq, CA (STN), REGISTRY (STN), WPI
 (DIALOG), BIOSIS (DIALOG)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO, 98/42840, A1 (ZYMOGENETICS, INC.), 01 October, 1998 (01.10.98), p.19, pp.54-58 & AU, 9865769, A & NO, 9904614, A & EP, 975760, A1 & BR, 9808059, A & CN, 1254375, A	1-32, 40-53
X	BLUET-PAJOT, M-T. et al., "Hypothalamic and hypophyseal regulation of growth hormone secretion", Cellular and Molecular Neurobiology (1998), Vol.18, No.1 pp.101-104, p.109	1, 5, 33-36, 39, 54, 56
P, X	KOJIMA, M. et al., "Ghrelin is a growth-hormone-releasing acylated peptide from stomach", NATURE (Dec.1999), Vol.402, No.9, pp.656-660	1-36, 39-54, 56
P, X	HOSODA, H. et al., "Purification and characterization of rat des-Gln ¹⁴ -Ghrelin, a second endogenous ligand for the growth hormone secretagogue receptor", J. Biol. Chem. (MAY, 2000), Vol.275, No.29, pp.21995-22000	1-36, 39-54, 56
P, X	WO, 99/63088, A2 (GENENTECH, INC.),	1-32, 40-53

Further documents are listed in the continuation of Box C. See patent family annex.

• Special categories of cited documents:	
• "A" document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
• "E" earlier document but published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
• "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
• "O" document referring to an oral disclosure, use, exhibition or other means	
• "P" document published prior to the international filing date but later than the priority date claimed	"&" document member of the same patent family

Date of the actual completion of the international search 17 October, 2000 (17.10.00)	Date of mailing of the international search report 24 October, 2000 (24.10.00)
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Name and mailing address of the ISA/ Japanese Patent Office	Authorized officer
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Facsimile No.	Telephone No.
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INTERNATIONAL SEARCH REPORT

International application No.

PCT/JP00/04907

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
	09 December, 1999 (09.12.99), & AU, 9943286	

INTERNATIONAL SEARCH REPORT

International application No.

PCT/JP00/04907**Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)**

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.: 37-39,55,57
because they relate to subject matter not required to be searched by this Authority, namely:
Claims 37, 38, 55 and 57 pertain to methods for treatment of the human body by therapy and thus relate to a subject matter which this International Searching Authority is not required to search.
2. Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

A. 発明の属する分野の分類 (国際特許分類 (IPC))

Int C17 C07K14/47, C12N15/12, C12N1/21, C12P21/02, C07K16/18, A61K38/18, A61P5/06, A61P19/08, A61K45/00, A61K48/00, G01N33/53

B. 調査を行った分野

調査を行った最小限資料 (国際特許分類 (IPC))

Int C17 C07K14/47, C12N15/12, C12N1/21, C12P21/02, C07K16/18, A61K38/18, A61P5/06, A61P19/08, A61K45/00, A61K48/00, G01N33/53

最小限資料以外の資料で調査を行った分野に含まれるもの

国際調査で使用した電子データベース (データベースの名称、調査に使用した用語)

SwissProt/PIR/GeneSeq, Genbank/EMBL/DBJ/GeneSeq, CA (STN), REGISTRY (STN), WPI (DIALOG), BIOSIS (DIALOG)

C. 関連すると認められる文献

引用文献の カテゴリー*	引用文献名 及び一部の箇所が関連するときは、その関連する箇所の表示	関連する 請求の範囲の番号
X	WO, 98/42840, A1 (ZYMOGENETICS, INC.) 1. 10月, 1998 (01. 10. 98) p. 19, p54-58 &AU, 9865769, A &NO, 9904614, A &EP, 975760, A1 &BR, 9808059, A &CN, 1254375, A	1-32, 40-53
X	BLUET-PAJOT, M-T. et al. "Hypothalamic and hypophyseal regulation of growth hormone secretion", Cellular and Molecular Neurobiology (1998) 第18巻, 第1号 p. 101-104, 109	1, 5, 33-36, 39, 54, 56

C欄の続きにも文献が列挙されている。

パテントファミリーに関する別紙を参照。

* 引用文献のカテゴリー

「A」特に関連のある文献ではなく、一般的技術水準を示すもの

「E」国際出願日前の出願または特許であるが、国際出願日以後に公表されたもの

「L」優先権主張に疑義を提起する文献又は他の文献の発行日若しくは他の特別な理由を確立するために引用する文献 (理由を付す)

「O」口頭による開示、使用、展示等に言及する文献

「P」国際出願日前で、かつ優先権の主張の基礎となる出願

の日の後に公表された文献

「T」国際出願日又は優先日後に公表された文献であって出願と矛盾するものではなく、発明の原理又は理論の理解のために引用するもの

「X」特に関連のある文献であって、当該文献のみで発明の新規性又は進歩性がないと考えられるもの

「Y」特に関連のある文献であって、当該文献と他の1以上の文献との、当業者にとって自明である組合せによって進歩性がないと考えられるもの

「&」同一パテントファミリー文献

国際調査を完了した日

17. 10. 00

国際調査報告の発送日

24.10.00

国際調査機関の名称及びあて先

日本国特許庁 (ISA/JP)

郵便番号 100-8915

東京都千代田区霞が関三丁目4番3号

特許庁審査官 (権限のある職員)

六笠 紀子

4B

9735

印

電話番号 03-3581-1101 内線 3448

C (続き) 関連すると認められる文献		関連する 請求の範囲の番号
引用文献の カテゴリー*	引用文献名 及び一部の箇所が関連するときは、その関連する箇所の表示	
P, X	KOJIMA, M. et al. "Ghrelin is a growth-hormone-releasing acylated peptide from stomach", NATURE (Dec. 1999) 第402巻, 第9号 p. 656-660	1-36, 39-54, 56
P, X	HOSODA, H. et al. "Purification and characterization of rat des-Gln ⁶ -Ghrelin, a second endogenous ligand for the growth hormone secretagogue receptor", J. Biol. Chem. (MAY, 2000) 第275巻, 第29号 p. 21995-22000	1-36, 39-54, 56
P, X	WO, 99/63088, A2 (GENENTECH, INC.) 9. 12月. 1999 (09. 12. 99) &AU, 9943286	1-32, 40-53

第1欄 請求の範囲の一部の調査ができないときの意見（第1ページの2の続き）
法第8条第3項（PCT17条(2)(a)）の規定により、この国際調査報告は次の理由により請求の範囲の一部について作成しなかった。

1. 請求の範囲 37, 38, 55, 57 は、この国際調査機関が調査をすることを要しない対象に係るものである。
つまり、
請求の範囲 37、38、55及び57は、人の身体の治療による処置方法であるから、
この国際調査機関が調査をすることを要しない対象に係るものである。

2. 請求の範囲 _____ は、有意義な国際調査をすることができる程度まで所定の要件を満たしていない国際出願の部分に係るものである。つまり、

3. 請求の範囲 _____ は、従属請求の範囲であってPCT規則6.4(a)の第2文及び第3文の規定に従って記載されていない。

第II欄 発明の単一性が欠如しているときの意見（第1ページの3の続き）

次に述べるようにこの国際出願に二以上の発明があるとこの国際調査機関は認めた。

1. 出願人が必要な追加調査手数料をすべて期間内に納付したので、この国際調査報告は、すべての調査可能な請求の範囲について作成した。
2. 追加調査手数料を要求するまでもなく、すべての調査可能な請求の範囲について調査することができたので、追加調査手数料の納付を求めなかった。
3. 出願人が必要な追加調査手数料を一部のみしか期間内に納付しなかったので、この国際調査報告は、手数料の納付のあった次の請求の範囲のみについて作成した。
4. 出願人が必要な追加調査手数料を期間内に納付しなかったので、この国際調査報告は、請求の範囲の最初に記載されている発明に係る次の請求の範囲について作成した。

追加調査手数料の異議の申立てに関する注意

- 追加調査手数料の納付と共に出願人から異議申立てがあった。
 追加調査手数料の納付と共に出願人から異議申立てがなかった。

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